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Introductory Remarks:

Session on Disease Conditions Predisposing Afflicted Individuals to the Toxic Effects of Pollutants

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Earlier papers have dealt with the effect of genetic makeup and age on response to pollutants, particularly at cellular and enzyme levels; the gut has been considered and, in relation to α_1-antitrypsin deficiency, the lung. The next paper considers the lung as the portal of entry, and in the two following papers as the site of attack as well. For these introductory remarks I have selected several points of current or special interest.

Seeing our lungs filter so much air the dose of any irritant or agent to which the lung is exposed may be greatly in excess of environmental concentration. The anatomical site at which a pollutant impinges is important; for the gaseous phase it is alveolar, for the particulate it may be alveolar or airway depending on particle size. In the alveoli it is mainly the macrophages that represent the respiratory defense mechanism, whereas in the airways it is mucociliary clearance. Mucus secretion, clearance, and bronchial muscle constriction each need to be assessed in relation to any irritant or pollutant.

Our understanding of the nonrespiratory functions of lung, to use the current shorthand, is proceeding fast. In this connection I commend to you a recent series of monographs of which Dr. Claude Lenfant is Executive Editor which deals with a fast-growing field and, although it is invidious perhaps to choose any of the nine that have appeared to date, I would especially mention Volumes 1, 4 and 5 as particularly relevant to the topic of this meeting: Immunologic and Infectious Reactions in the Lung (*1*), Metabolic Functions of the Lung (*2*) and Respiratory Defense Mechanisms (*3*).

In considering populations at risk, it is important to look at recent studies of childhood disease. Our understanding of lung growth and its impairment and remodelling by disease are relevant to reduced pulmonary function reserve as seen in the adult (*4*). Burrows and his colleagues (*5*) have shown a close relationship between history of childhood respiratory disorders and prevalence of cough and sputum in the adult and also ventilatory impairment. Their study was concerned with 2526 adults over the age of 20 years who had been questioned in relation to childhood illness. In young adults, the impairment is mild but they show an excessive decline in function with advancing years and with cigarette use. These are relatively mild changes as revealed by epidemiological studies but it is, in large part, with such populations that discussions of groups at risk need to be be concerned.

There is also another group of children and adolescents who in the near future will be at risk in the industrial market. Correction of genetic defects, or of developmental anomalies present at birth, may "cure" the patient but it should be accepted that such patients are still at risk (*4, 5*). The size of the population may be small, but they are a group for which failure to continue careful follow-up may be critical in outcome. A radiograph after correction of diaphragmatic hernia (*6*) may be normal; a child may be healthy and yet function studies can detect that the ipseleteral lung, at least, is not normal (*7*). Mary Ellen Wohl and her colleagues have shown reduced perfusion to the ipseleteral side after correction of a hernia. Although the chest x-ray is normal, sometimes the left lower lobe is sufficiently emphysematous to appear translucent in the radiograph (*8, 9*).

Hematological correction of infants with rhesus isoimmunization is possible and yet it is likely that there has been impairment of lung development

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during intra-uterine life (*10*). Airway number is reduced which points to disturbance before the sixteenth week of intra-uterine development. Follow-up studies in this group have not been undertaken to determine the state of the lungs' function.

Prematurity of increasingly severe degree is now associated with survival but the nature of the lung function of such subjects (*11–13*). It would seem appropriate that follow-up of children with these conditions should be undertaken but such prospective studies are time-consuming. Perhaps a registry, at least some record, should be kept of such patients so that when and if it seems desirable, follow-up is possible. A history of childhood respiratory problem or infection should be part of any questionnaire in which a population risk is being studied.

There is a somewhat different category of children with childhood diseases which should be studied more carefully, and in which the demand is probably more urgent. Children with bronchiolitis (*14*), with cystic fibrosis, or children who have had asthma during childhood or have developed localized hyperlucency in the radiograph after childhood infection, are all those in whom exposure to industrial irritants or to an inclement environment may be serious. These patients are unusual and rare in relation to the overall population in the industrial field, but from the point of view of the individual subject it is an important group. They are a group of individuals for whom a risk, acceptable in regard to the large part of the adult working population, should not be considered acceptable.

A word on experimental studies of chronic bronchitis (*15, 16*). Respiratory function studies are increasingly sensitive and able to detect early functional changes. Taking clinical and experimental studies together, it seems that hypertrophy of submucosal glands and increase of secretory cell number in the surface epithelium, particularly of the small airways, are the main structural changes in chronic bronchitis. There is definite and measurable increase in the secretory cells before the symptom of sputum production is apparent: both the number of cells and their state of activity influence the functional result. These changes in structure have been produced by irritants, by drugs, and by infection. Previous incidents of exposure to such agents may, therefore, have modified the airway epithelium and its response to a new irritant. Recently Jones (*15*) has investigated the early effect of tobacco on airway surface epithelium and has shown the extreme speed of development of new secretory cells. Exposure to smoke, from cigarettes delivered for 5 hr each day produced 48 hr from the start an increase in goblet cells in the small airways equivalent to that produced by 2–6 weeks exposure. The speed with which these changes develop is matched only by the speed with which the intracellular glycoprotein also shows a shift.

Mucociliary clearance depends on epithelial integrity and the amount of secretion on the surface. Prostaglandin $F_{2\alpha}$ produces an epithelial secretion of glycoprotein with virtually no serum component although in most human disease sputum usually has a serum component as well (*17*). Studies of the physicochemical properties of the sputum produced by patients with asthma show that sputum from intrinsic asthma patients differs from that of extrinsic asthma; that produced by the former resembles that of chronic bronchitis rather than that of extrinsic asthma. It is desirable in epidemiological studies of patients with asthma to distinguish the intrinsic from the extrinsic. This classification might not be acceptable to all but the essential feature, from the point of view of this discussion, is that patients who, between the attacks of asthma, continue to produce sputum regularly, come into the category of those with chronic bronchitis as well. The studies of Lopez-Vidriero (*17*) show that the sputum features of patients with intrinsic asthma more nearly resemble those of chronic bronchitis.

There is considerable variation in the mucociliary clearance as between normal individuals and between normal individuals and those with disease. It is important to know whether the rate and speed of normal clearance is in any way bound up with the subsequent development of disease.

The hazard of tobacco smoking is an extremely significant factor in the susceptibility of an individual to a pollutant. Some of you may have seen that the city of Alexandria, Virginia, will recruit only fire-fighters who promise not to smoke on or off duty. It is now well established that tobacco smoking modifies the effect of asbestos and of α_1-antitrypsin deficiency. When we relate hazard to chronic bronchitis, it is well to remember that in most of these subjects it is chronic bronchitis that is induced by tobacco smoke, making it necessary to refer back to the habit of the individual.

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